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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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151	7590	03/13/2006	EXAMINER	
HOFFMANN-LA ROCHE INC. PATENT LAW DEPARTMENT 340 KINGSLAND STREET NUTLEY, NJ 07110			ROBINSON, HOPE A	
			ART UNIT	PAPER NUMBER
			1656	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/634,477

Applicant(s)

LEHMANN ET AL.

Examiner

Hope A. Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed September 2, 2005 on December 16, 2005, is acknowledged.
2. Claim 2 is cancelled. Claims 16-26 have been added. Claims 1 and 3-26 are pending and are under examination.

Priority

3. This application claims foreign priority to EP 02019100.3, filed August 29, 2002, however, it is noted that a certified copy of the priority document is missing from the application, thus the conditions under 35 U.S.C. 119 (a-d) have not been met.

Drawing

4. The drawing filed on December 16, 2005 has been accepted by the Examiner.

Withdrawn-Claim Objection

5. Previous objection to claims are withdrawn by virtue of submission of an amendment, which cancelled or amended the claims.

Duplicate Claims, Warning

6. Applicant is advised that should claims 3-12 be found allowable, claims 17-26 will

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be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim.

See MPEP § 706.03(k).

Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3, 5-17 and 19-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a method of treating disturbances in iron distribution by administering human erythropoietin protein and claim 1 for example is defined solely by a function as the claim does not recite a reference structure for said

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protein. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). Further claim 5 is directed to a modified protein structure and the claim does not set forth where in the sequence the modification will occur. In addition, the claims are directed to an erythropoietin protein conjugate, said conjugate comprising an erythropoietin protein having at least one free amino group and having the *in vivo* biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human erythropoietin and analogs thereof ...", thus the claims encompass fragments (emphasis added). The specification does not demonstrate retention of function for the fragments to demonstrate possession of the genus as claimed in the invention.

In addition, the claim recites "human erythropoietin and analogs thereof which have a sequence of human erythropoietin modified by the addition of from 1 to 6 glycosylation sites or a rearrangement of at least one glycosylation site" and there is no indicia in the claims as to where in the claims this will occur or if the modification is to the human erythropoietin or to the analogs thereof. In addition, the specification at paragraph 0015 contemplates adding amino acids to achieve additional glycosylation sites. The claims do not provide adequate description to indicate that the addition or rearrangement of glycosylation sites results in analogs thereof or correlate structure with function. Additionally, paragraph 0018 of the specification indicate that the analogs

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may be generated by site-directed mutagenesis having additions, deletions, or substitutions of amino acid residues that increase or alter sites that are available for glycosylation. Note also that there is no limit on the number of "free amino group" the structure can possess. A skilled artisan cannot envision the detailed chemical structures of all the analogs encompassed in the claims. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus.

A representative number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In addition, the claims are directed to a pharmaceutical composition (see claims 13-15), however, the claims do not recite a pharmaceutically acceptable carrier or excipient. Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

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8. Claims 1, 3, 5-17 and 19-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treating disturbances in iron distribution herein and the disclosure in the art, does not reasonably provide enablement for said method employing analogs thereof of the administered protein (EPO). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)). The factors most relevant to the instant invention are discussed below.

The claims broadly recite a treatment method comprising administration of EPO and no structure is provided for said protein to correlate the structure with the function. In addition, the breath of the claims encompass an unspecified amount of analogs. There is no limit on the number of "free amino group" the structure can possess and the claims encompass addition of glycosylation sites via additional amino acid residues or rearrangement of existing sites. The instant specification at paragraph 0015

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contemplates adding amino acids to achieve additional glycosylation sites. Paragraph 0018 of the specification indicate that the analogs may be generated by site-directed mutagenesis having additions, deletions, or substitutions of amino acid residues that increase or alter sites that are available for glycosylation. No correlation is made between structure and function to indicate retention of function or the specified activity. Thus, undue experimentation would be required to practice the claimed invention commensurate in scope with the claims.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity

and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected. The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. Yamaguchi et al. disclose that the elimination of three N-glycosylation sites decreased EPO production to 10% of that of the wild-type EPO and found that said mutation changed affinity of EPO to the receptor (The Journal of Biological Chemistry, vol. 266, no. 30, pages 20434-20439, 1991). The skilled artisan would recognize the high degree of unpredictability that all the analogs encompassed in the claims would retain the recited function. The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence

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and result in certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of analogs. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...".

Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test analogs of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible analogs to

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find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 3-15 and 17-26 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claims 3-15 and 17-26 lack clear antecedent basis for "the erythropoietin protein" as claim 1 recites "human erythropoietin".

Claims 5 and 19 lack clear antecedent basis for "human erythropoietin modified by the addition of from 1 to 6 glycosylation sites", as independent claim 1 is directed to a "human erythropoietin protein", not a mutant.

Claims 8-12 and 22-26 lack clear antecedent basis as the claims recite "the erythropoietin protein is a conjugate" and independent claim 1 recites, "human erythropoietin protein", thus there is no recitation of "conjugate".

Claims 13-15 are indefinite because the claims recite a pharmaceutical composition, however, the composition does not have a carrier.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 1, 3-4 and 17-18 are rejected under 35 U.S.C. 102(a) as being anticipated by Silverberg et al. (Nephrol. Dial. Transplant., vol. 18 (1), pages 141-146, 2003).

Silverberg et al. disclose a study to investigate the effect of correcting anemia with subcutaneous erythropoietin in patients with type II diabetes (claim 1, page 141 of the reference). As the claims recite "alfa or beta", said property is an inherent property of EPO (claim 3). Further, the structure reported in claim 4 is simply another property the EPO. Therefore, the limitations of the claims are met by this reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains.
Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

11. Claim 1, 4-15 and 18-26 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Silverberg et al. (Nephrol. Dial. Transplant., vol. 18 (1), pages 141-146, 2003) in view HOFFMANN-LA ROCHE (EP 1064 951, January 3, 2001 (cited on IDS - March 21, 2005).

Silverberg et al. disclose a study to investigate the effect of correcting anemia with subcutaneous erythropoietin in patients with type II diabetes (claim 1). As the claims recite "alfa or beta", said property is an inherent property of EPO (claim 3). Further, the structure reported in claim 5 is simply another property the EPO.

As the reference by Silverberg et al. teach erythropoietin, claims reciting epoetin alfa or beta are obvious as these are properties of erythropoietin. Schreiber et al. does not teach erythropoietin with modifications by adding 1 to 6 glycosylation sites.

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However, HOFFMANN-LA ROCHE teach glycosylation of erythropoietin (see page 2 of the reference); and pegylated erythropoietin conjugates and the chemical structures claimed (see claim 4 and 7-15, pages 1-5 of the reference).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have a method of treating disturbances in iron in a patient suffering from diabetes comprising administering human erythropoietin because Silverberg et al. teach a method to treat anemia (iron disturbance) employed in patients suffering from type II diabetes, by administration of erythropoietin. In addition, HOFFMANN-LA ROCHE teach a glycosylated, pegylated and conjugated erythropoietin, and the chemical structures claimed in the instant invention. One of ordinary skill in the art would be motivated to combine the teachings of the references because erythropoietin is known in the art to treat anemia (iron disturbance) in patients. Further, HOFFMANN-LA ROCHE teach erythropoietin for the same purpose and that as a conjugate to PEG an increased half-life is achieved. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

Basis For NonStatutory Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

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USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 3-15 and 17-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-14 of copending Application No. 10/706,701. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The copending application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from heart disease comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta; SEQ ID NO:1; a modification of 1 to 6 glycosylation sites; a darbepoetin; pegylated; and a conjugate having a particular structure. The instant application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from diabetes (type II) comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta; SEQ ID NO:1; a modification of 1 to 6 glycosylation sites; a darbepoetin; pegylated; and a conjugate having a particular structure. The copending application claims differ from the instant application in that the patient is suffering from heart disease, whereas the instant application patient is suffering from diabetes, however, the methods have one step, administering erythropoietin, thus the resulting effect will be the same. Moreover, the art generally recognizes that heart disease is a risk with diabetes, for example type II diabetes. In fact, studies have shown that there is a five-fold increase in the risk for heart disease in women with diabetes, thus the administration of erythropoietin is critical to both diseases claimed in the applications. Note that the Silverberg et al. reference of record is treating a patient having anemia, congestive heart failure and type II diabetes with EPO. Therefore, the two sets of claims differ in scope but are obvious one over the other, as the intended use does not materially change the composition administered.

14. Claims 1, 3-12 and 17-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4-15 of copending Application No. 11/013,560. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The copending application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from chronic inflammatory intestinal disease comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta; SEQ ID NO:1; a modification of 1 to 6 glycosylation sites; a darbepoetin; pegylated; and a conjugate having a particular structure. The instant application claim 1 is directed to a method of treating disturbances in iron distribution in a patient suffering from diabetes (type II) comprising administering a therapeutically effective amount of human erythropoietin. The dependent claims hereto are directed to an erythropoietin that is epoetin alfa or beta; SEQ ID NO:1; a modification of 1 to 6 glycosylation sites; a darbepoetin; pegylated; and a conjugate having a particular

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structure. The instant application claims differ from the copending application in that the patient is suffering from diabetes, whereas the copending application patient is suffering from chronic inflammatory intestinal disease, however, the methods have one step, administering erythropoietin, thus the resulting effect will be the same. Thus, the two sets of claims differ in scope but are obvious one over the other, as the intended use does not materially change the composition administered.

Response to Arguments

16. The response filed on December 16, 2005 has been considered, however, is not fully persuasive. Note the rejections remain under 35 U.S.C. 112, first and second paragraphs and 103. New grounds of rejection have been instituted under 35 U.S.C. 112, first paragraph enablement and 102 (a) for the reasons stated above.

Regarding the rejection under 35 U.S.C. 112, first paragraph written description, applicant on page 12 state that the essential goal of the written description requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed. Applicant is reminded that "an applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997)". It is further stated that there is a strong presumption that an adequate written description of the claimed invention is present

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when the application is filed. Applicant states that the examiner has the initial burden of presenting evidence or reasoning to explain why the persons skilled in the art would not recognize in the disclosure a description of the invention as defined by the claims. It is stated that a pharmaceutically acceptable carrier or excipient is conventional in the art and known to those of ordinary skill in the art.

Applicant's statements have been considered, however, are not persuasive. The prior art teaching can enable the instant specification, however, cannot provide missing description. A pharmaceutically composition requires a pharmaceutically acceptable carrier or excipient. A skilled artisan knows that water is a carrier, whether or not that is the carrier applicant intended in the claimed invention should be set forth in the specification. Additionally, the discussion provided in the instant specification (for example at paragraphs 0090-0091) is exemplary and not limiting, thus does not breathe life into the claims. Further, *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written

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description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993).

Moreover, the rejection has been amended to clarify the issues raised and the written description rejection is not based solely on the composition as stated by applicant. Applicant's discussion focused on the claimed composition, however, the rejection discussed the analogs encompassed by the claims, which applicant's response did not address. Applicant also state that the PTO itself does not require a recitation of a pharmaceutically acceptable carrier in classification of certain pharmaceutical composition. This argument is not germane to the issues raised and applicant is reminded that each application is considered on its own merits.

Note that the rejection under 35 U.S.C. 112 second paragraph remains. Applicant state that they have amended the claims to recite "human erythropoietin protein", however, no such amendment was made (see page 14 of the response). Applicant state that claim 1 and claim 8 for example both encompass an EPO protein which is modified, said modification makes up the conjugate. Claim 1 reads on a full-length, wild type EPO and does not read on mutants/analogues of said protein, thus the rejection remains. In addition, applicant states that claims reciting the composition are definite. The rejection remains as the claims are considered to be incomplete, absent a pharmaceutically acceptable carrier. Limitations in the specification and the art cannot be read into the claims. Further, the instant specification discussion pertaining to the claimed composition is exemplary and not limiting, thus, the metes and bounds of the

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claim is undefined. It is not clear from the claim or the instant specification how applicant intends to transport the claimed composition to achieve the goal of treating patients experiencing disturbances of iron distribution while concurrently having type II diabetes. Additionally claims remain indefinite for the recitation of "conjugate" as there is no basis in claim 1. Modifications cannot be read into independent claim 1. It is suggested that an independent claim is written with all the pertinent information from claim 1.

On pages 14-15 applicant argues that "an applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. Accordingly, in reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim appraises one of ordinary skill in the art of its scope and, therefore, serves the notice function required...by providing clear warning to others as to what constitutes infringement of the patent". This argument is not persuasive. Applicant does not have a claim that recites "A composition comprising", applicant has a claim that recites "A pharmaceutical composition" which requires a pharmaceutically acceptable carrier. The carrier is necessary it is not a matter of preference or alternative expression, the composition claim is broader and encompasses said carrier as well as other components, a pharmaceutical composition does not garner the same scope. Applicant also state that there are over 6200 patents that have been granted with pharmaceutical composition claims without recitation of a carrier and/or excipient. This

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argument is not persuasive as each application is treated on its own merits, however, to address applicant's statement there are 856,765 patents issued reciting "a pharmaceutical composition comprising a pharmaceutically acceptable carrier". Thus, for the reasons herein and stated above the rejections remain.

Applicant's arguments regarding the rejection under 35 U.S.C. 103 have been considered, however are moot as the rejection has been amended removing the Bosman et al. reference based on amendments made to the claims. With regard to the rejections under 35 U.S.C. 103 Obvious-type double patenting the applicant regards these rejections as premature and request that they be held in abeyance until there is notification of allowable subject matter. The rejections have been made of record as they should during prosecution and are stated as being provisional rejections because the applications are copending. The rejections remain because a terminal disclaimer was not filed.

Conclusion

17. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr,

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can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner

HOPE ROBINSON
PATENT EXAMINER

[Signature]
3/3/06